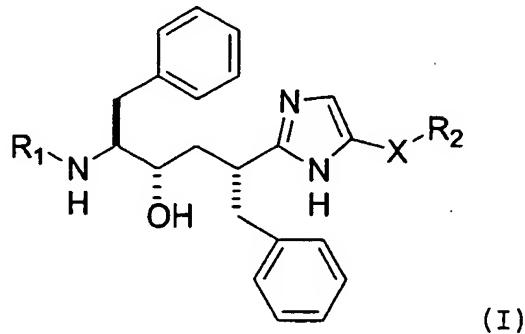


CLAIMS

We claim:

1. A method of treating or preventing Alzheimer's disease
5 in a subject in need of such treatment comprising administering a
therapeutically effective amount of a compound of Formula (I) or a
pharmaceutically acceptable salt thereof:



10 wherein R₁ is

- a) Cbz-Val;
- b) Cbz-Ala;
- c) Cbz; or
- d) Boc;

15 R₂ is

- a) H;
- b) C₁₋₆ alkyl, alkenyl, or alkynyl; or
- c) cycloalkyl; and

X is

20

- a) C=O; or
- b) (CH₂)OH.

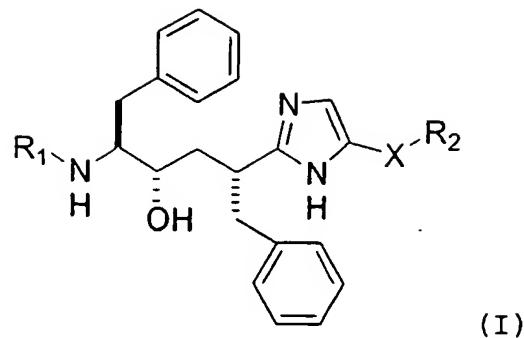
2. A method of treating Alzheimer's disease in a subject in
need of such treatment comprising administering to the subject a

compound disclosed in claim 1, or a pharmaceutically acceptable salt thereof.

3. A method of treating Alzheimer's disease by modulating
5 the activity of beta amyloid converting enzyme, comprising
administering to a subject in need of such treatment a compound
disclosed in claim 1, or a pharmaceutically acceptable salt
thereof.

10 4. The method according to claim 1, further comprising the
administration of a P-gp inhibitor, or a pharmaceutically
acceptable salt thereof.

15 5. A method of treating a subject who has, or in preventing
a subject from getting, a disease or condition selected from the
group consisting of Alzheimer's disease, for helping prevent or
delay the onset of Alzheimer's disease, for treating subjects with
mild cognitive impairment (MCI) and preventing or delaying the
onset of Alzheimer's disease in those who would progress from MCI
20 to AD, for treating Down's syndrome, for treating humans who have
Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type,
for treating cerebral amyloid angiopathy and preventing its
potential consequences, i.e. single and recurrent lobar
hemorrhages, for treating other degenerative dementias, including
25 dementias of mixed vascular and degenerative origin, dementia
associated with Parkinson's disease, dementia associated with
progressive supranuclear palsy, dementia associated with cortical
basal degeneration, or diffuse Lewy body type of Alzheimer's
disease and who is in need of such treatment which includes
30 administration of a therapeutically effective amount of a compound
of formula (I), or a pharmaceutically acceptable salt thereof:



wherein R₁ is

- 5 a) Cbz-Val;
- b) Cbz-Ala;
- c) Cbz; or
- d) Boc;

R₂ is

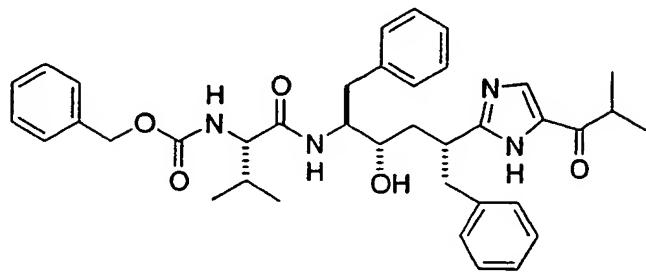
- 10 a) H;
- b) C₁₋₆ alkyl, alkenyl, or alkynyl; or
- c) cycloalkyl; and

X is

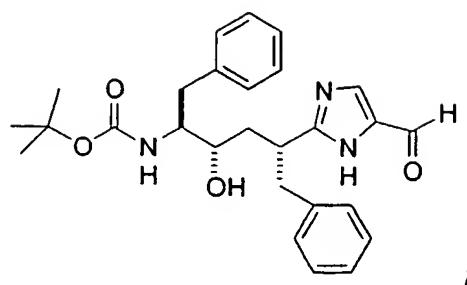
- a) C=O; or
- b) (CH₂)OH.

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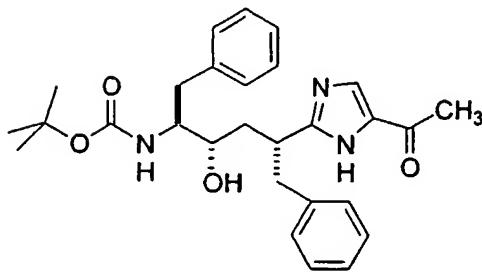
6. The method according to any of claim 1-5 wherein the compound of formula (I) is selected from the group consisting of:



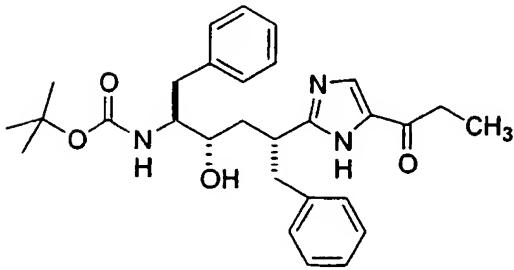
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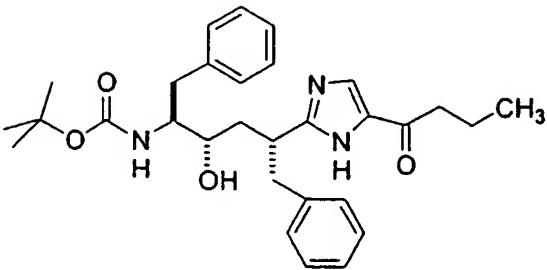


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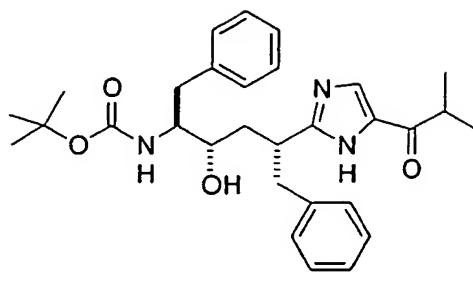


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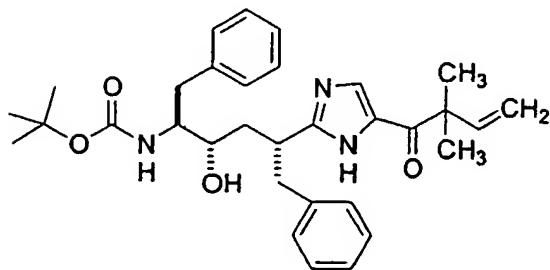
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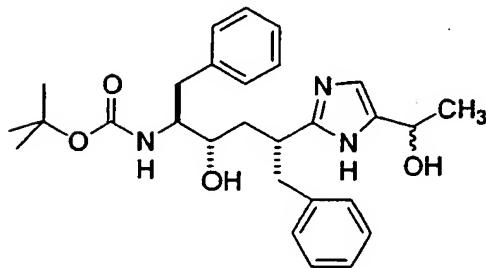
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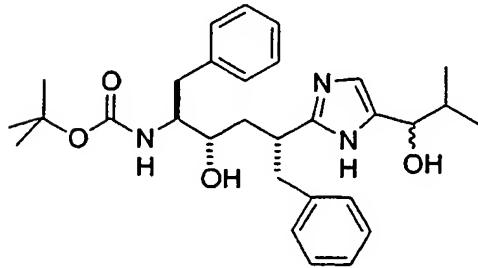
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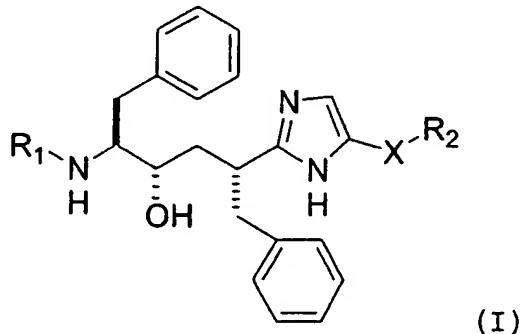


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10 or pharmaceutically acceptable salts thereof.

7. A method of treating or preventing Alzheimer's disease in a subject in need of such treatment comprising administering a therapeutically effective amount of a composition comprising one or more pharmaceutically acceptable carriers and a compound of
 5 Formula (I) or a pharmaceutically acceptable salt thereof:



wherein R₁ is

- a) Cbz-Val;
- 10 b) Cbz-Ala;
- c) Cbz; or
- d) Boc;

R₂ is

- a) H;
- 15 b) C₁₋₆ alkyl, alkenyl, or alkynyl; or
- c) cycloalkyl; and

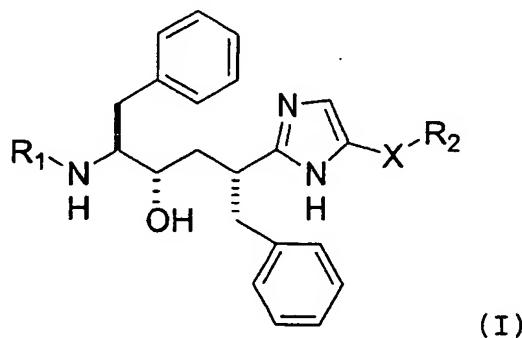
X is

- a) C=O; or
- b) (CH₂)OH.

20

8. Use of a compound of Formula (I) in the manufacture of a medicament for the treatment of conditions selected from the group consisting of Alzheimer's disease, mild cognitive impairment (MCI) Down's syndrome, Hereditary Cerebral Hemorrhage with Amyloidosis
 25 of the Dutch-Type, cerebral amyloid angiopathy, degenerative

dementias, including dementias of mixed vascular and degenerative origin, dementia associated with Parkinson's disease, dementia associated with progressive supranuclear palsy, dementia associated with cortical basal degeneration, or diffuse Lewy body 5 type of Alzheimer's disease:



wherein R₁ is

10 a) Cbz-Val;
b) Cbz-Ala;
c) Cbz; or
d) Boc;

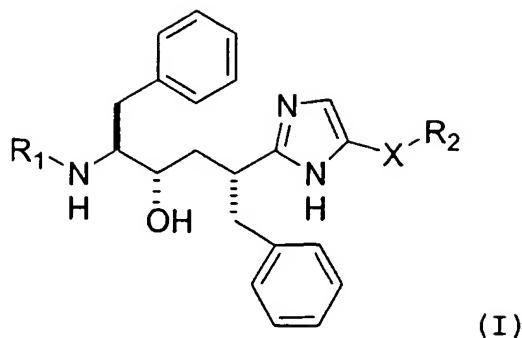
R₂ is

15 a) H;
b) C₁₋₆ alkyl, alkenyl, or alkynyl; or
c) cycloalkyl; and

X is

20 a) C=O; or
b) (CH₂)OH.

9. A method for inhibiting beta-secretase activity, comprising contacting an effective amount for inhibition of a compound of formula (I):



wherein R_1 is

- 5 a) Cbz-Val;
- b) Cbz-Ala;
- c) Cbz; or
- d) Boc;

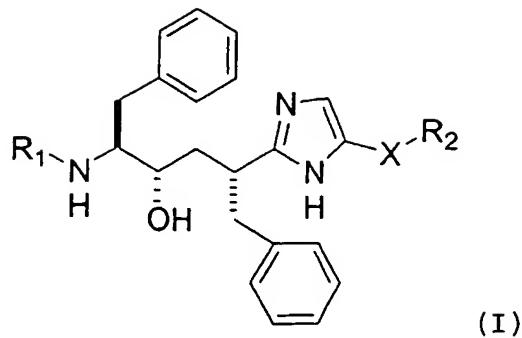
R_2 is

- 10 a) H;
- b) C_{1-6} alkyl, alkenyl, or alkynyl; or
- c) cycloalkyl; and

X is

- a) $C=O$; or
- b) $(CH_2)_2OH$.

15 10. A method for inhibiting cleavage of an amyloid precursor protein (APP) isotype at a site in the APP isotype that is susceptible to cleavage, comprising contacting said APP isotype with an effective cleavage inhibitory amount of a compound of
20 formula (I):



wherein R_1 is

- 5 a) Cbz-Val;
- b) Cbz-Ala;
- c) Cbz; or
- d) Boc;

R_2 is

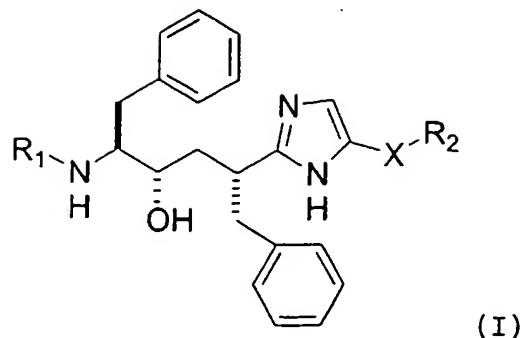
- a) H;
- 10 b) C_{1-6} alkyl, alkenyl, or alkynyl; or
- c) cycloalkyl; and

X is

- a) $C=O$; or
- b) $(CH_2)_2OH$.

15

11. A method for inhibiting production of amyloid beta peptide (A beta) in a cell, comprising administering to said cell an effective inhibitory amount of a compound of formula (I):



wherein R_1 is

- a) Cbz-Val;
- 5 b) Cbz-Ala;
- c) Cbz; or
- d) Boc;

R_2 is

- a) H;
- 10 b) C_{1-6} alkyl, alkenyl, or alkynyl; or
- c) cycloalkyl; and

X is

- a) $C=O$; or
- b) $(CH_2)_2OH$.

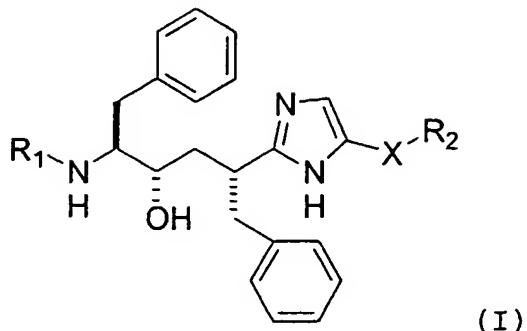
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12. The method of claim 11, wherein the cell is an animal cell.

20 13. The method of claim 12, wherein the animal cell is a mammalian cell.

14. The method of claim 13, wherein the mammalian cell is human.

15. A composition comprising beta-secretase complexed with a compound of formula (I):



5

wherein R₁ is

- a) Cbz-Val;
- b) Cbz-Ala;
- c) Cbz; or
- d) Boc;

10

R₂ is

- a) H;
- b) C₁₋₆ alkyl, alkenyl, or alkynyl; or
- c) cycloalkyl; and

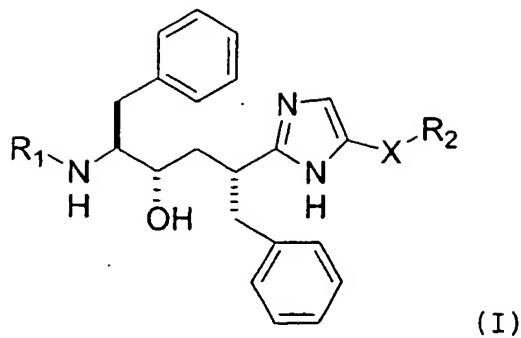
15 X is

- a) C=O; or
- b) (CH₂)OH.

16. A method for producing a beta-secretase complex comprising the composition of claim 15.

17. A method for inhibiting the production of beta-amyloid plaque in an animal, comprising administering to said animal an effective inhibiting amount of a compound of formula (I):

25



wherein R_1 is

- a) Cbz-Val;
- 5 b) Cbz-Ala;
- c) Cbz; or
- d) Boc;

R_2 is

- a) H;
- 10 b) C_{1-6} alkyl, alkenyl, or alkynyl; or
- c) cycloalkyl; and

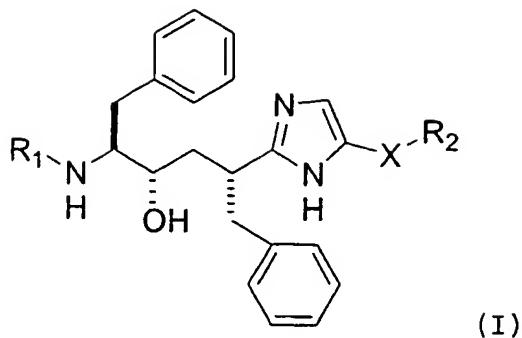
X is

- a) $C=O$; or
- b) $(CH_2)_2OH$.

15

18. The method of claim 17, wherein said animal is a human.

19. A method for treating or preventing a disease characterized by beta-amyloid deposits on or in the brain, 20 comprising administering to a subject in need of such treatment or prevention an effective therapeutic amount of a compound of formula (I):



wherein R₁ is

- 5 a) Cbz-Val;
- b) Cbz-Ala;
- c) Cbz; or
- d) Boc;

R₂ is

- 10 a) H;
- b) C₁₋₆ alkyl, alkenyl, or alkynyl; or
- c) cycloalkyl; and

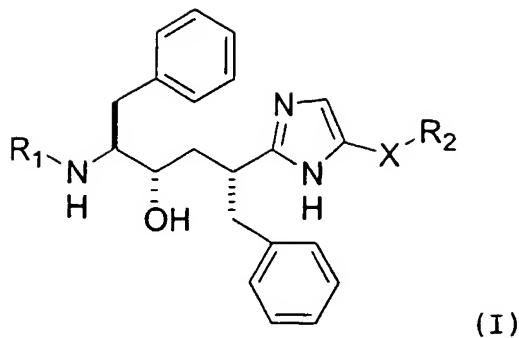
X is

- a) C=O; or
- b) (CH₂)OH.

15

20. A method of treatment according to any of claims 1-5, further comprising administration of one or more therapeutic agents selected from the group consisting of an antioxidant, an anti-inflammatory, a gamma secretase inhibitor, a neurotrophic 20 agent, an acetyl cholinesterase inhibitor, a statin, an A beta peptide, and an anti-A beta peptide.

21. Use of a compound of Formula (I):



wherein R₁ is

- a) Cbz-Val;
- 5 b) Cbz-Ala;
- c) Cbz; or
- d) Boc;

R₂ is

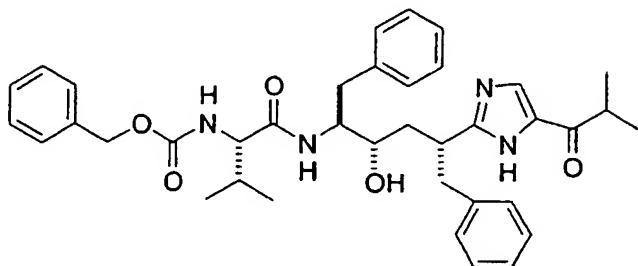
- a) H;
- 10 b) C₁₋₆ alkyl, alkenyl, or alkynyl; or
- c) cycloalkyl; and

X is

- a) C=O; or
- b) (CH₂)OH;

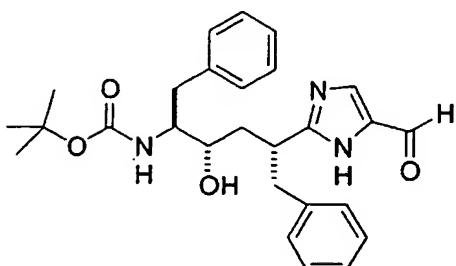
15 for the manufacture of a medicament for the treatment of conditions selected from the group consisting of: Alzheimer's disease, mild cognitive impairment (MCI) Down's syndrome, Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type, cerebral amyloid angiopathy, degenerative dementias, including 20 dementias of mixed vascular and degenerative origin, dementia associated with Parkinson's disease, dementia associated with progressive supranuclear palsy, dementia associated with cortical basal degeneration, or diffuse Lewy body type of Alzheimer's disease.

22. The use of a compound of formula I according to claim 21, wherein the compound of formula I is selected from the group consisting of:

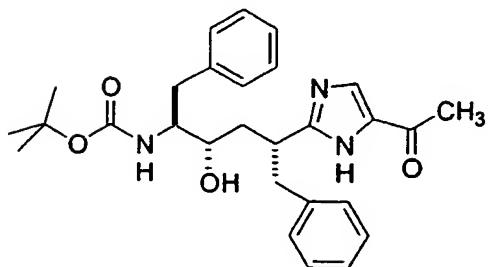


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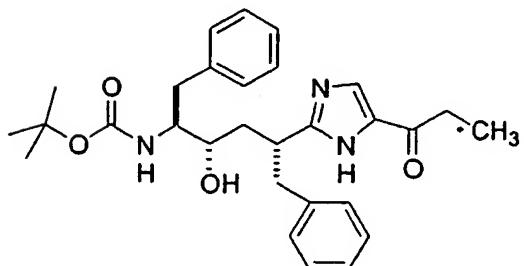


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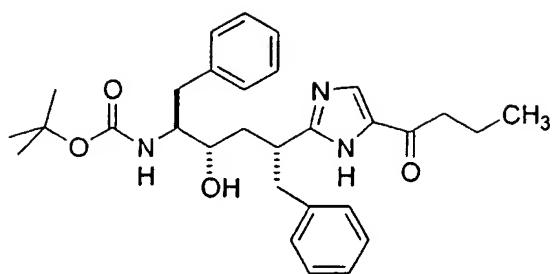


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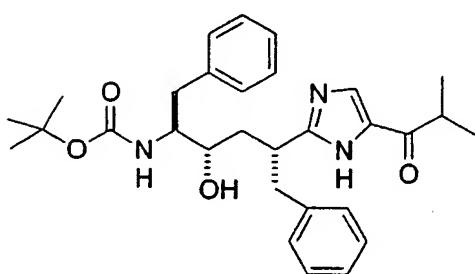
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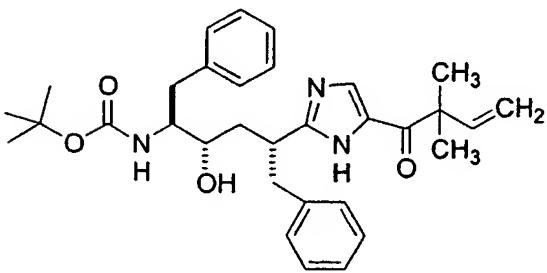
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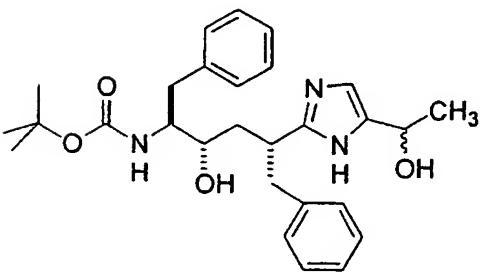


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